

IN THE UNITED STATES PATENT OFFICE

Continuation Applic. of U.S. Application
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CUSTOMER NO. 23607

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Title: EMULSION PRECONCENTRATE COMPRISING A
CYCLOSPORIN AND ACETYLATED MONOGLYCERIDE

Inventor: Bernard Charles Sherman

Examiner: Vickie Kim

Group Art Unit: 1615

PRELIMINARY AMENDMENT

February 15, 2001

VIA COURIER

The Commissioner of Patents
UNITED STATES PATENT OFFICE
2011 South Clark Place
Crystal Plaza 2, Room 1B03
Arlington, Virginia, U.S.A. 22202

Dear Sir:

Applicants respectfully request that the following submissions be entered as a Preliminary Amendment.

IN THE ABSTRACT

No changes.

IN THE DISCLOSURE

No changes.

IN THE CLAIMS

Before calculating the fee for filing the Continuation Application, please cancel claims 2 to 14 originally filed in United States Patent Application No. 09/403,660 and add new Claims 15 to 21 as follows:

15. A pharmaceutical composition in the form of an emulsion preconcentrate comprising a cyclosporin dissolved in acetylated monoglyceride lipophilic solvent, and a surfactant.

16. The composition of claim 1 or 15 in the form of a microemulsion preconcentrate.

17. The composition of claim 1 or 15 wherein the acetylated monoglyceride is a fully acetylated monoglyceride prepared from unsaturated monoglyceride.

18. The composition of claim 1 or 15 wherein the surfactant is selected from the group of a polyoxyethylene glycolated natural , hydrogenated vegetable oil, polyoxyl 40 hydrogenated castor oil, and a polyoxyethylene-sorbitan-fatty ester.

19. The composition of claim 1 or 15 comprising two surfactants, one of which is a polyoxyethylene glycolated natural or hydrogenated vegetable oil and the second of which is a polyoxyethylene-sorbitan-fatty acid ester.

20. The composition of claim 15 further comprising a hydrophilic organic solvent miscible with the acetylated monoglyceride lipophilic solvent.

21. The composition of claim 20 wherein said hydrophilic organic solvent is selected from the group of ethanol, propylene glycol, propylene carbonate, benzyl alcohol, and polyethylene glycol having mean molecular weight of less than about 1000.

REMARKS

Originally filed Claim 1 of United States Patent Application No. 09/403,660 remains in this Continuation Application. In the prior parent case Claims 1-14 stood rejected under 35 USC 103 as allegedly being obvious over Illum et al. Applicant therefore submitted an extensive response which is repeated in part here with the exception of the amendments made to the claims in that case.

Before commencing any arguments in relation to the Examiner's rejection under 35 U.S.C. 103, Applicant would respectfully like to review some of the excerpted jurisprudence from which he will draw inferences and conclusions when formulating specific remarks relating to the prior art of record within the instant application.

OBVIOUSNESS

The traditional test enunciated in Graham vs. John Deere Company 383 U.S. 1, 148 U.S.P.Q. 459 1966, for Section 103 nonobviousness requires the fact finder to make several determinations. The test provides that the scope and content of the prior art be determined, the differences between the prior art and the claims at issue be ascertained, and the level of ordinary skill in the pertinent art be resolved. Thus, the patentability of the claims at hand must stem from the fact that the specific combination of the claimed elements was not disclosed in the prior art and the additional allegation that the specific combination of claimed elements was nonobvious to one of ordinary skill in the art.

As further defined in Jacobson Bros. Incorporated vs. United States at 512 F.2d 1065, 185 U.S.P.Q. 168 (Ct. Cl. 1975), in reviewing the level of skill in the art, one must consider the prior art approaches employed, the types of problems encountered in the art, the rapidity with which innovations are made, the sophistication of the technology involved, and the educational background of those actively working in the field. In considering the aforementioned factors, one may develop a picture of what the level of skill of the ordinary person skilled in the art may be.

The question of nonobviousness is a simple one to ask but difficult to answer. The person of ordinary skill in the art at the time of the invention is presumed to have before him all of the relevant prior art. The difficulty which attaches to an honest attempt to answer this question can be attributed to the strong temptation to reply on hindsight while undertaking this evaluation; combining the right references in the right way so as to achieve the result of the claims in suit. Monday morning quarterbacking is quite improper when resolving the question

of nonobviousness in a court of law. What matters in Section 103 nonobviousness determination is whether a person of ordinary skill in the art having all of the teachings of the references before him is able to produce the structure defined by the claim.

Applicant again respectfully contends that none of the references either alone or in combination, would render the present invention obvious under 35 U.S.C. 103 to one skilled in the art. The "picking and choosing" and combining of references in the rejection clearly presents a case of an improper hindsight reconstruction. An improper hindsight reconstruction is one in which a rejection is construed from isolated teachings of the prior art without considering the overall context within which those teachings are presented. A rejection based on 35 U.S.C. 103 clearly must rest on a factual basis and these facts must be interpreted without hindsight reconstruction of the invention from the prior art. The case law has long upheld these principles, see e.g. In re Mercier, 185 U.S.P.Q. 774 (C.C.P.A. 1975), In re Rice, 178 U.S.P.Q. 478 (C.C.P.A. 1973), and In re Warner et al, 154 U.S.P.Q. 173 (C.C.P.A. 1967).

Likewise, the courts have long held that "obvious to try" is not the standard of 35 U.S.C. 103 and not the test of patentability, and further that it is impermissible within the framework of 35 U.S.C. 103 to "pick and choose" from parts of reference to construct a rejection. See e.g. In re Lunsford, 148 U.S.P.Q. 721 (C.C.P.A. 1966), In re Dien, 152 U.S.P.Q. 550 (C.C.P.A. 1967), In re Lindell, 155 U.S.P.Q. 521 (C.C.P.A. 1967), In re Marzocchi et al, 169 U.S.P.Q. 367 (C.C.P.A. 1971), In re Kamm et al, 172 U.S.P.Q. 298 (C.C.P.A. 1972), In re Antonie, 195 U.S.P.Q. 6 (C.C.P.A. 1977), In re Goodwin et al, 198 U.S.P.Q. 1 (C.C.P.A. 1978), and In re Yates, 211 U.S.P.Q. 1149 (C.C.P.A. 1981).

The Examiner is also reminded of a comment by Mr. Justice Hand 1935 B. G. Corporation vs. Walter Kiddle Company, 79 F.2d 20, 22 (2d Cir. 1935),

"all machines are made up of the same elements; rods, pawls, pistons, pitmans, journals, toggles, gears, cams and the like all acting their part as they always do and always must. All compositions are made of the same substances retaining their fixed chemicals properties. But the elements are capable of an infinity of permutations and the selection of that group which proves serviceable to a given need may require a high degree of originality. It is that act of selection which is the invention."

This comment was reinforced in Reeves Instruments vs. Beckman Instruments 444 F.2d 263, 270 170 U.S.P.Q. 74 (9th Cir. 1971) and Republic Industries vs. Schlage Block Company U.S.P.Q. (7th Cir. 1979).

Applicant further submits that a correct and recent statement of the law of obviousness is presented within Windsurfing International Inc. and Fred Ostermann GMBH et al, in the Re: Sernaker reasoning of the Court of Appeal 702 F.2d 989 (Federal Circuit 1983) when it was concluded that the following related test are appropriate standards against which to make an obviousness determination:

- (a) whether a combination of the teachings of all or any of the references would have suggested (expressly or by implication) the possibility of achieving further improvement by combining such teachings along the line of the invention in suit, and
- (b) whether the claimed invention achieved more than a combination which any or all of the prior art references suggested expressly or by reasonable implication.

Referring to the Windsurfing case, it was determined that although the test (a) was satisfied, the test (b) was not satisfied because the prior art references in combination do not make an invention obvious unless something in the prior art references would suggest the advantage to be derived from combining their teachings. It was therefore concluded that the patented invention in the Windsurfing case resulted in more than a combination suggested by any of the prior art references.

Finally the Examiner is respectfully directed toward Anderson Black Rock Incorporated vs. Pavement Salvage Company Inc. 396 U.S. 57 1969, wherein it was stated that each element of the invention performed the same function together that it performed separately in the prior art. Thus the combination of elements only accomplished the performance of all of its known functions without any synergistic result and thus would be rendered unpatentable.

It is not always necessary to show the nonobviousness of the claimed invention to overcome a §103 rejection or attack. Sometimes what is alleged to be a prima facie case of obviousness is no such thing, because it is a defective or specious showing. Then there is no need at all for the applicant or patentee to go forward to show nonobviousness. All he need do is demonstrate the impropriety of the alleged prima facie obviousness showing. Some examples of such specious showings (by no means exhaustive) and the appropriate responses are set forth below. When an attempt is made to combine two references A and B, or to change a single reference, a prima facie case of obviousness has not been established if:

- (1) A and B could not or would not be physically combined in an operative fashion or to produce the desired result by a person of ordinary skill without use of the patentee's teachings. *In re Lintner*, 458 F.2d 1013, 173 USPQ 560, 562 (CCPA 1972); *In re Regel*, 526 F.2d 1399, 188 USPQ 136 (CCPA 1975); *In re Jansson*, 609 F.2d 996, 203 USPQ 976 (CCPA 1979).
- (2) The intended purpose or function of either A or B, or both, is destroyed by their combination. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).
- (3) No suggestion why or reasons or motivation for combining A and B appears explicitly or implicitly in either A or B, or both in combination. *In re Clinton*, 527 F.2d 1226, 188 USPQ 365 (CCPA 1976).
- (4) A and B are from such diverse arts (i.e., either or both are nonanalogous art to the claimed invention) that a person of ordinary skill in the claimed art would not look to those arts to solve the problem treated by the claimed invention. *In re Pagliaro*, 657 F.2d 1219, 210 USPQ 888 (CCPA 1981); *In re*

Wood, 599 F.2d 1032, 202 USPQ 171 (CCPA 1979); *In Re Horn*, 203 USPQ 969 (CCPA 1979).

(5) A and B, or the single reference, does not teach the source of the problem, and the recognition of the source of the problem is what is unobvious. *Eibel Process Co. v. Minnesota and Ontario Paper Co.*, 261 US 45 (1923); *In re Spinnoble*, 405 F.2d 578, 160 USPQ 237 (CCPA 1969); *In re Peehs*, 612 F.2d 1287, 204 USPQ 835 (CCPA 1980).

Once a prima facie obvious rejection is shown to be proper, and the applicant (or patentee) introduces rebuttal evidence, the examiner (or trial court) must forget that, or ignore the fact that, a prima facie case had been established. The issue of obviousness must be examined afresh. All that the prima facie showing was good for was to force the applicant or patentee to come forward with evidence of nonobviousness in technological form or the objective indicia, or both.

The systematic investigation of nonobviousness includes as relevant evidence the objective indicia of nonobviousness, the so-called "secondary considerations." Those relevant indicia include:

- (a) Long felt but unsatisfied need for the invention while the needed implementing arts and elements had long been available;
- (b) Appreciation that a problem existed and what the problem was were theretofore unseen by those skilled in the art;
- (c) Substantial attempts by those skilled in the art to fill the need of (a) or to cope with the difficulties extant because of failure to understand the problem of (b);
- (d) Commercial success of the invention causally related to the invention itself, rather than to companion factors such as advertising or attractive packaging;
- (e) Replacement in the industry of the prior art devices by the patented invention;
- (f) Prompt copying of the patentee's invention by competitors, as distinguished from their independent development thereof;
- (g) Acquiescence by the industry to the patent's validity by honoring the patent through taking licenses or not infringing the patent, or both;
- (h) Teaching away from the technical direction in which the patentee went by those skilled in the art;
- (i) Unexpectedness of the results of the invention to those skilled in the art; and
- (j) Disbelief and incredulity on the part of those skilled in the art that the patentee's approach worked.

See *Hodosh v. Block Drug Co., Inc.*, 786 F.2d 1136, 1143 n⁵, 229 U.S.P.Q. 182, 187 n⁵ (Fed. Cir. 1986) (listing the "following tenets of patent law that must be adhered to when applying § 103: (1) the claimed invention must be considered as a whole . . . (2) the references must be considered as a whole and suggest the desirability and thus the obviousness of making the combination . . . (3) the references must be viewed without the benefit of hindsight vision afforded by the claimed invention . . . (4) 'ought to be tried' is not the standard with which obviousness

is determined . . . and (5) the presumption of validity remains constant and intact throughout litigation"). For a topical outline and case tables covering the decisions of the Federal Circuit, see the separate *Guide to the Patent-Related Decisions of the Court of Appeals for the Federal Circuit* in Volume 6 of this treatise. See also Dunner, ed., "The United States Court of Appeals for the Federal Circuit - Its First Three Years," 13 AIPLA Q.J. 185 (1985); Mintz & Racine, "Anticipation and Obviousness in the Federal Circuit," 13 AIPLA Q.J. 195 (1985).

In Re: Fritch, 23 U.S.P.Q. 2d 1780 (Fed. Cir. 1992)

"Wilson and Hendrix fail to suggest any motivation for, or desirability of, the changes espoused by the Examiner and endorsed by the Board. Here, the Examiner relied upon hindsight to arrive at the determination of obviousness. It is impermissible to use the claimed invention as an instruction manual or 'template' to piece together the teachings of the prior art so that the claimed invention is rendered obvious. The court has previously stated that '[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."

A synopsis of highlight §103 points and cases of the Federal Circuit follows.

Most if not all inventions are combinations of known elements; there is solely one standard of nonobviousness for all types of inventions. *Medtronic, Inc. v. Cardiac Pacemakers, Inc.*, 721 F.2d 1563, 720 USPQ 97 (Fed. Cir. 1983); *Fromson v. Advanced Offset Plate, Inc.*, 720 F.2d 1565, 219 USPQ 1137 (Fed. Cir. 1983); *In re Grasselli*, 713 F.2d 731, 218 USPQ 769 (Fed. Cir. 1983); *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Environmental Designs, Ltd. v. Union Oil*, 713 F.2d 693, 218 USPQ 865 (Fed. Cir. 1983). Chief Judge Markey, writing for the court in *Fromson v. Advanced Offset Plate*, 755 F.2d 1549, 1556, 225 USPQ 26, 31 (Fed. Cir. 1985), took the trial court to task for its statement that the patent in suit is a "combination patent comprised exclusively of old elements." Chief Judge Markey observed that "only God works from nothing. Men must work with old elements." Judge Markey cited his article, *Why not the Statute?*, 65 JPOS 331 (1983); the old Testament could properly be relied upon as authority as well.

In ascertaining the differences between the prior art and the claims at issue (the second factual inquiry of *Graham v. John Deere*), it is essential to consider the claims at issue as "the invention as a whole," as required by §103:

- a. It is essential to consider all elements of the claimed invention; it is impermissible to compare the prior art with what the viewer interprets the "gist" of the invention to be. *Perkin-Elmer Corp. v. Computervision Corp.*, 732 F.2d 888, 221 USPQ 669 (Fed. Cir. 1984); *Jones v. Hardy*, 727 F.2d 1524, 1527-28, 220 USPQ 1021, 1024 (Fed. Cir. 1984) ("Reducing a claimed invention to an 'idea', and

then determining patentability of the 'idea' is error."). See also, *W.L. Gore & Associates v. Garlock*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983); *ACS Hospital Systems v. Montefiore Hospital*, 732 F.2d 1572, 221 USPQ 929 (Fed. Cir. 1984); *Litton Industrial Products v. Solid State Systems Corp.*, 755 F.2d 158, 225 USPQ 34 (Fed. Cir. 1985).

b. It is impermissible to ignore the advantages, properties, utilities, and unexpected results flowing from the claimed invention; they are part of the invention as a whole. *Fromson v. Advanced Offset Plate*, 755 F.2d 1549, 225 USPQ 26 (Fed. Cir. 1985); *In re Piasecki*, 745 F.2d 1468, 223 USPQ 785 (Fed. Cir. 1984); *Schenck, A.G. v. Norton Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983); *In re Sernaker*, 702 F.2d 989, 217 USPQ 1 (Fed. Cir. 1983).

Criteria to be considered in determining the level of ordinary skill in the art (the third factual inquiry of *Graham v. John Deere*), as set forth in *Environmental Designs, Ltd. v. Union Oil*, 713 F.2d 693, 696, 218 USPQ 865, 868 (Fed. Cir. 1983), are:

- i. the educational level of the inventor;
- ii. type of problems encountered in the art;
- iii. prior art solutions to those problems;
- iv. rapidity with which innovations are made;
- v. sophistication of the technology; and
- vi. educational level of active workers in the field.

The prior art (item iii.) is a good indicator of the level of skill -- often it is a level inadequate to solve the problem the claimed invention successfully resolved. However, it may be that given the problem, an untutored layman (perhaps a district court judge) would immediately come up with a solution that those skilled (or expert) in the art would reject because of technical impediments not appreciated or appreciable by a layman. *Litton Industrial Products v. Solid State Systems*, 755 F.2d 158, 225 USPQ 34 (Fed. Cir. 1985) the inquiry is not what would have been obvious "to the judge or to the common layman").

The objective indicia of nonobviousness (the "secondary considerations" of *Graham v. John Deere*) are usually the most important items of evidence available and are properly viewed as a "fourth" factual inquiry in the *Graham v. John Deere* investigation. *Simmons Fastener Corp. v. Illinois Tool Works*, 739 F.2d 1573, 1575, 222 USPQ 744, 746 (Fed. Cir. 1984). Finding obviousness through hindsight (i.e., after the fact of the invention and with the teachings of the inventor available) is impermissible and refuted by the objective indicia of nonobviousness. *In re Piasecki*, 745 F.2d 1468, 223 USPQ 785 (Fed. Cir. 1984). *In re Sernaker*, 702 F.2d 989, 217 USPQ 1 (Fed. Cir. 1983).

Neither the PTO nor a trial court may decide the issue of obviousness without including in its evaluation the objective evidence of nonobviousness. It is impermissible for a trier of fact to say that the claimed invention is obvious and thus the evidence of nonobviousness in the form of objective indicia need not be

considered. It is a requirement of due process of law that all evidence on nonobviousness, including the "secondary considerations," be weighed before reaching an ultimate conclusion on §103. *Simmons Fastener*, supra; *Piasecki*, supra; *Sernaker*, supra; *In re Fielder*, 471 F.2d 640, 644, 176 USPQ 300, 303 (CCPA 1973); *In re Palmer*, 451 F.2d 1100, 172 USPQ 126 (CCPA 1971).

It is well settled that obviousness under § 103 can not be established by combining the teachings of the prior art to obtain the claimed invention, absent some teachings, suggestion, or incentive supporting the combination. See *In Re: Geiger*, 2 USPQ 2d 1276 (Fed. Cir. 1987). By the same token, the Examiner can not pick and chose among the individual elements of assorted prior art references, to recreate the claimed invention. To the contrary, the Examiner has the burden to show some teachings or suggestion in the reference to support their use in the particular claimed combination. See *Smithkline Diagnostics Inc. vs. Helena Laboratories Corp.*, 8 USPQ 2d 1468 (Fed. Cir. 1988).

In fact it is well established that for a combination of references to render an invention obvious, it must be obvious that the references can be combined; *In Re Avery* 186 U.S.P.Q.161 (CCPA 1975). The references themselves and not in retrospect, must suggest what has to be done. *In Re: Skoll* 187 USPQ 481 (CCPA 1975). There must be some reason for the combination other than hindsight gleaned from their invention itself. *Interconnect Planning Corp. vs. Feil*, 774 F. 2d 1132, 1134 (Fed. Cir. 1985). See also *Panduit Corp. vs. Dennison Mfg. & Co.*, 810 F. 2d 1561, 1568 (Fed. Cir. 1988) where the court said:

"Elements of separate prior art patents cannot be combined when there is no suggestion of such combination anywhere in those patents".

Although the Examiner suggests that the structure could readily be modified to form a combination of the claims at issue, the mere fact that the prior art could be so modified would not have made the modification obvious unless the prior art suggested the desirability of the modification. Please See *In Re: Gordon* 733 F. 2d 900-902, 221 USPQ 1125, 1127 (Fed. Cir. 1984); *In Re: Grabiak*, 769 F. 2d 729, 731, 226 USPQ 870, 872 (Fed. Cir. 1985).

Clearly, the prior art does not suggest or provide any reason or motivation to make such a modification as purported by the Examiner. With reference to *In Re: Regal*, 526 F. 2d 1399, 1403 n. 6, 188 USPQ 136, 139 n. 6 (CCPA 1975).

"There must be some logical reason apparent from positive, concrete evidence of record which justifies a combination of primary and secondary references".

In Re: Geiger, 815 F. 2d 686, 688, 2 USPQ 2d 1276, 1278 (Fed. Cir. 1987) (obviousness can not be established by combining pieces of prior art absence some "teachings, suggestion, or incentive supporting the combination"): *In Re: Cho*. 813 F. 2d 378, 382, 1 USPQ 2d 1662, 1664 (Fed. Cir. 1987)("discussing the Board's holding that the artisan would have been motivated to combine the references").

Therefore, it Applicant's view there is no evidence of motivation in the prior art, either within the references themselves, or knowledge generally available to one of ordinary skill in the art, to make the purported changes suggested by the Examiner to arrive at the claimed subject matter.

Further in re Vaeck , 947 F.2d 488,20 USPQ2d 1438 (Fed. Cir. 1991):

"Rejection of claimed subject matter as obvious under 35 USC 103 in view of combination of prior art references requires consideration of whether prior art would have suggested to those of ordinary skill in art that they should make claimed composition or device, or carry out claimed process, and whether prior art would also have revealed that such person would have reasonable expectation of success; both suggestion and reasonable expectation of success must be founded in prior art, not in applicant's disclosure."

It is also submitted that the following Cases update and reinforce Applicant's previously discussed excerpted case law with reference to obviousness.

Referring again to the in the In Re Sernaker Decision before the Court of Appeals, Federal Circuit 702 F 2d 989, 217 USPQ 1 it was stated therein;

"When one skilled in the art at the time of the invention is considering all the prior art in combination, we wholly fail to perceive what more he would have found. The most that would have appeared to have been suggested was the use of transfer prints on rough substrates by which, no doubt, a variety of designs might have been achieved. Mating or registering are suggested nowhere in the prior art. Therefore, it does not show how to approach the results this inventor achieved. No prior art suggests expressly or by implication keeping the print off the substrate and providing a "sculptured" embroidery in a pattern to mate and register with the print."...

"The lesson of this case appears to be that prior art references in combination do not make an invention obvious unless something in the prior art references would suggest the advantage to be derived from combining their teachings. It does not appear from the opinion that the inventor actually did anything not disclosed somewhere in the prior art references, and in that regard the case was less favorable for unobviousness than the case at bar, where none of the prior art references disclosed an embroidery inserted between the print and the substrate, "registered" or mated the print with the embroidery, not the substrate, and transferred the print to the insert, not to the substrate."

It is Applicant's view that the above-mentioned excerpted sections from the In Re Sernaker decision, reinforces describe the meanings of the aforementioned broadly accepted test, as to whether a combination of the teachings of all or any of the references would have suggested (expressly or by implication) the possibility of achieving further improvement by combining such teachings along line of the invention in suit, (b) whether the claimed invention achieved more than a combination which any or all of the prior art references suggested, expressly or by reasonable implication.

Further in the Re Pleuddemann Decision of August the 3, 1990 before the Court of Appeals, Federal Circuit, 910 F 2d 823, 15 USPQ 2d 1738 the following comment is found:

"In Kuehl the court said, 475 F.2d at 664-665, 177 USPQ at 255:

The test under §103 is whether in view of the prior art the invention as a whole would have been obvious at the time it was made, and the prior art here does not include the zeolite, ZK-22. The obviousness of the process of cracking hydrocarbons with ZK-22 as a catalyst must be determined without reference to knowledge of ZK-22 and its properties. So judged, the process of the appealed claims would not have been obvious. (Emphasis ours).

In the present case likewise, §103 obviousness of claims 26 and 27 depends on the obviousness of using appellant's new compounds, which constitute the essential limitation of the claims, in light of the prior art. That being so, the board's hindsight comparison of the functioning of the new compounds with the functioning of the compounds of the prior art was legal error. It uses appellant's specification teaching as though it were prior art in order to make claims to methods of bonding/priming using his admittedly novel compounds appear to be obvious."

Referring now to the Decision of the Court of Appeals Federal Circuit In Re Bond, decided on August 3, 1990, found at 910 F 2d 831, 15 USPQ 1566, it is stated:

"We are convinced that this holding does not recognize that there are critical differences between the claimed invention and the prior art. See *Graham v. John Deere Co.*, 383 U.S. 1, 17-18, 148 USPQ 459, 467 (1966) (the difference between the claimed invention and the prior art is one of the four factual inquiries pertinent to any obviousness inquiry under 35 U.S.C. §103). It also does not reflect the admonition of this court that "obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or incentive supporting the combination." *Carella v. Starlight Archery and Pro Line Co.*, 804 F. 2d 135, 140, 231 USPQ 644, 647 (Fed. Cir. 1886); see also *ACS Hosp. Sys., Inc. v. Montefiore Hosp.*, 732 F. 2d 1572, 1577, 221 USPQ 929, 933 (Fed. Cir. 1984). The Board's analysis is a classical example of a hindsight reconstruction of the claimed invention."

Referring to the Court of Appeal's, Federal Circuit Decision of April 3, 1989, In Re Laskowski, 10 USPQ 2d 1397, there is found an extensive discussion which Applicant submits should be the test for determining obviousness, in view of combining prior art references.

"Although the Commissioner suggests that Hoffman could readily be modified to form the Laskowski structure, 'the mere fact that the prior art could be so modified would not have made the modification obviousness unless the prior art suggested the desirability of the modification.' In re Gordon, 733 F. 2d 900, 902, 221 USPQ 1125, 1127

(Fed. Cir. 1984). See also, e.g., *Interconnect Planning Corp., v. Feil*, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985); *In re Grabiak*, 769 F.2d 729, 731, 226 USPQ 870, 872 (Fed. Cir. 1985); *In re Sernaker*, 702 F.2d 989, 994, 217 USPQ 1, 5 (Fed. Cir. 1983).

The prior art does not suggest Laskowski's modification of the Hoffman band saw wheel, or provide any reason or motivation to make that modification. *In re Regel*, 526 F.2d 1399, 1403 n.6, 188 USPQ 136, 139 n.6 (CCPA 1975) ('there must be some logical reason apparent from positive, concrete evidence of record which justifies a combination of primary and secondary references') (citing *In re Stemniski*, 44 F.2d 581, 170 USPQ 343 (CCPA 1971)). We agree with the Commissioner that the suggestion to modify the Hoffman structure need not be found in Hoffman. In this case, however, the only source of the suggestion is Laskowski; there is no prior art teaching that would provide the motivation of using a loosely fitting tire, rising above the pulley flanges, to support the saw blade. See *In re Geiger*, 815 F.2d 686, 688, 2 USPQ 2d 1276, 1278 (Fed. Cir. 1987) (obviousness can not be established by combining pieces of prior art absent some 'teaching, suggestion, or incentive supporting the combination'); *In re Cho*, 813 F.2d 378, 382, 1 USPQ 2d 1662, 1664 (Fed. Cir. 1987) (discussing the Board's holding that 'the artisan would have been motivated' to combine the references); *In re Deminiski*, 796 F.2d 436, 443, 230 USPQ 313, 316 (Fed. Cir. 1986) (impropriety of hindsight reconstructions); *In re Donohue*, 766 F.2d 531, 534, 226 USPQ 619, 622 (Fed. Cir. 1985) (referring to the 'suggestion or motivation to combine teachings' in rejections for obviousness) (citing *In re Samour*, 571 F.2d 559, 563, 197 USPQ 1, 4-5 (CCPA 1978)); *In re Clinton* 527 F.2d 1226, 1228, 188 USPQ 365, 367 (CCPA 1976) (holding that 'a person of ordinary skill in the art would have had sufficient motivation to combine' the separate steps); *In re Boe*, 505 F.2d 1297, 1299, 184 USPQ 38, 40 (CCPA 1974) (discussing 'the main motivation for combining' two prior art references)."

Further in considering simplicity and improvements:

"Simplicity is no bar to invention if steps taken are not obvious to ordinary mechanic.-- *Blish, Mize & Silliman Hardware Co., v. Time Saver Tools, Inc.* (CA 10) 111 USPQ 6."

"Gross appearance is not reliable measure of invention; apparent simplicity of patented device points toward presence of invention where device for years escaped prior workers skilled in the art and made the difference between impractical suggestions and useful improvement accepted as such be those in art to which device relates.-- *Appleton Electric Co. V. Wagner Malleable Iron Co.* (DC NIII) 109 USPQ 341."

"Ease and cheapness of manufacture are not ordinarily the kind of new result upon which invention can be predicated, but they are proper evidence to consider in evaluating usefulness of patent in its field.-- *Fischer & Porter Co. v. Brooks Rotameter Co.* (DC EPa) 95 USPQ 37,"

"Narrowness and simplicity do not bar patentability; despite apparent simplicity of device, there may be invention where it

appears that industry had for many years sought satisfactory device, that numerous devices had been tried and abandoned, and that patented device met with hearty response on part of users; one who produces patentable new results, the simplicity of which effects savings of time and costs, not suggested by prior references, may be entitled to patent. --Schneider Metal Mfg. Co. v. Ernest, Inc. (DC WPAa) 94 USPQ 109."

"Simplicity of patented structure does not negative invention.-- Baltz v. Botto (DC WTenn) 111 USPQ 376."

"It does not necessarily negative invention or patentability that, viewed after disclosure and explanation by applicant, device seems simple and such as should have been obvious to those in field; simplicity may even be some evidence of invention.--In re Osplack (CCPA) 93 USPQ 306."

"Patent will not be invalidated simply because it embodies solution that seems simple and obvious with benefit of hindsight. ---Omark Industries, Inc. v. Textron, Inc. (CA 9, 1982) 216 USPQ 749."

"Court will not engage in hindsight; fact that invention seems simple after it is made does not determine question; many of most beneficial patents would be stricken down if this were rule. --Johns-Manvill Corp. v. Guardian Industries Corp. (DC EMich, 1983) 221 USPQ 319."

"Simple: and "obvious" are not synonymous terms. --EWP Corp. v. Reliance Universal, Inc. (DC SOhio, 1983) 221 USPQ 542."

"Invention's simplicity is not to be equated with obviousness. --Ethyl Molded Products Co. v. Betts Packaging Inc. (DC EKy, 9/2/88) 0 USPQ 2d 1001."

"Invention need not be complex or superior to previous devices in order to be non-obvious. --Demaco Corp. v. F. Von Langsdorff Licensing Ltd. (CA FC, 6/21/88) 7 USPQ 2d 122."

Applicant respectfully submits that the cited art does not teach or suggest acetylated monoglycerides as an advantageous lipophilic solvent for cyclosporin emulsion preconcentrates. It is used by Illum et al in examples 1 and 3 in combination only as a co-solvent for itraconazole but not as a lipophilic solvent. Nor is it suggested anywhere in Illum to be used as a lipophilic solvent and particularly with a cyclosporin. Respectfully the Examiner is using Applicant's teaching to reach this conclusion which relies on hindsight to do so.

Nowhere in Illum is there taught either of the following:

1. "A pharmaceutical composition in the form of an emulsion preconcentrate comprising a cyclosporin dissolved in a solvent comprising acetylated monoglycerides, a hydrophilic organic solvent and a surfactant."
and

15. "A pharmaceutical composition in the form of an emulsion preconcentrate comprising a cyclosporin dissolved in acetylated monoglyceride lipophilic solvent, and a surfactant."

Clearly Illum et al teaches the use of Vitamin E as a solubilizer. His formulations in examples 1 and 3 do not provide emulsion or microemulsion preconcentrates, which is the subject matter of the invention. Indeed, Illum clearly teaches that the formulations of these examples have to be mixed and heated to 60° to get dispersion, whereas those of the present invention will self-disperse when ingested.

Again nowhere does Illum et al teach a pharmaceutical composition in the form of a emulsion pre-concentrate including a cyclosporin dissolved in acetylated monoglyceride lipophilic solvents and a surfactant together, nor does Illum et al use acetylated monoglycerides at all in a self-emulsifying preconcentrates, even without cyclosporin. Nor is there any motivation to do so from the teachings of Illum. The Examiner is relying on a high level of skill in the art and a 20/20 hindsight reconstruction to arrive at this conclusion.

See In Re: Fritch, 23 U.S.P.Q. 2d 1780 (Fed. Cir. 1992)

"Wilson and Hendrix fail to suggest any motivation for, or desirability of, the changes espoused by the Examiner and endorsed by the Board. Here, the Examiner relied upon hindsight to arrive at the determination of obviousness. It is impermissible to use the claimed invention as an instruction manual or "template" to piece together the teachings of the prior art so that the claimed invention is rendered

obvious. The court has previously stated that "[o]ne cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."

Further the Examiner is referred to the following excerpted case law recently reviewed.

In Re: Rouffet, 47 U.S.P.Q. 2d 1453 (Fed. Cir. 1998)

"As this court has stated, "virtually all [inventions] are combinations of old elements." Environmental Designs, Ltd. v. Union Oil Co., 713 F.2d 693, 698, 218 USPQ 865, 870 (Fed. Cir. 1983); see also Richdel, Inc. v. Sunspool Corp., 714 F.2d 1573, 1579-80, 219 USPQ 8, 12 (Fed. Cir. 1983) ("Most, if not all, inventions are combinations and mostly of old elements."). Therefore an examiner may often find every element of a claimed invention in the prior art. If identification of each claimed element in the prior art were sufficient to negate patentability, very few patents would ever issue. Furthermore, rejecting patents solely by finding prior art corollaries for the claimed elements would permit an examiner to use the claimed invention itself as a blueprint for piecing together elements in the prior art to defeat the patentability of the claimed invention. Such an approach would be "an illogical and inappropriate process by which to determine patentability." Sensonics, Inc. v. Aerosonic Corp., 81 F.3d 1566, 1570, 38 USPQ 2d 1551, 1554 (Fed. Cir. 1996).

To prevent the use of hindsight based on the invention to defeat patentability of the invention, this court requires the examiner to show a motivation to combine the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.

This court has identified three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art. In this case, the Board relied upon none of these. Rather, just as it relied on this high level of skill in the art to overcome the differences between the claimed invention and the selected elements in the references, it relied upon the high level of skill in the art to provide the necessary motivation. The Board did not, however, explain what specific

understanding or technological principle within the knowledge of one of ordinary skill in the art would have suggested the combination. Instead, the Board merely invoked the high level of skill in the field of art. If such a rote invocation could suffice to supply a motivation to combine, the more sophisticated scientific fields would rarely, if ever, experience a patentable technical advance. Instead, in complex scientific fields, the Board could routinely identify the prior art elements in an application, invoke the lofty level of skill, and rest its case for rejection. To counter this potential weakness in the obviousness construct, the suggestion to combine requirement stands as a critical safeguard against hindsight analysis and rote application of the legal test for obviousness.

Because the Board did not explain the specific understanding or principle within the knowledge of a skilled artisan that would motivate one with no knowledge of Rouffet's invention to make the combination, this court infers that the examiner selected these references with the assistance of hindsight. This court forbids the use of hindsight in the selection of references that comprise the case of obviousness. See In re Gorman, 933 F.2d 982, 986, 18 USPQ 2d 1885, 1888 (Fed. Cir. 1991). Lacking a motivation to combine references, the Board did not show a proper prima facie case of obviousness. This court reverses the rejection over the combination of King, Rosen and Ruddy."

The Examiner states that it would have been obvious to modify the composition of Illum and select cyclosporine as a main drug dissolved in acetylated monoglycerides as main oil solvent. However, Illum et al teaches the use of Vitamin E, not acetylated monoglycerides, the reference does not use acetylated monoglycerides, as a main oil solvent. Clearly this is a 20/20 hindsight reconstruction adopted by the Examiner. Picking elements from Illum et al and arriving at Applicant's claims is improper since clearly the motivation for one skilled in the art is lacking in Illum to do so and in fact Illum points in another direction.

The Examiner indicates it would have been obvious to use acetylated monoglycerides because it is better than pure vegetable oil to enhance solubility of cyclosporine. But there is no teaching in Illum clearly setting this allegation out. The Examiner's 20/20 hindsight reconstruction is quite apparent and relies heavily on her incorrectly assumed high level of skill of one of

ordinary skill in the art. The use of acetylated monoglycerides as lipophilic solvents for a cyclosporin is simply not taught in the Illum reference and **was not known before Applicant taught it**. It was certainly not known that acetylated monoglycerides are not only good solvents for cyclosporin but also more easily dispersible in water, making it a better choice as lipophilic solvents in a cyclosporin emulsion preconcentrate than any other component for that particular use disclosed in the art.

Specifically referring to the Examiner's comments on page 3 of her report of October 3, 2000 in the parent case, there is a considerable of reliance on the level of skill of one of ordinary skill in the art to support the Examiner's allegations of the present invention being obvious to those of ordinary skill in the art. First of all, (i) the ordinary person skilled in the art would have to select cyclosporin as a main drug and somehow reach the conclusion that (ii) it should be dissolved in an acetylated monoglyceride rather than Vitamin E contrary to the teachings of Illum. Clearly there is no understanding in Illum that the acetylated monoglycerides will function as a lipophilic solvent. (iii) Then one of ordinary skilled in the art, continuing with the Examiner's alleged obviousness rejection would have to be motivated to use the acetylated monoglyceride as a lipophilic solvent when nowhere in the Illum reference is there taught such use, although the Examiner has concluded fourthly, (iv) that such use would fall within the level of one of ordinary skill in the art that they would be motivated to do so having knowledge that, and this is the Examiner's conclusion, (v) the acetylated monoglyceride is formulated better than pure vegetable oil to enhance the solubility of cyclosporin, and (vi) that one of ordinary skill in the art would expect a reasonable chance of success when this activity is performed. As set out above there are six steps to be taken by one of ordinary skill in the art to arrive at the Examiner's conclusion and purportedly at Applicant's formulation from the teachings of Illum. Respectfully, the Examiner is incorrect and again referring to

the above referenced court case for the motivation to be there, and to combine with the reference it must come from 1) the nature of the problem to be solved; 2) the teachings of the prior art; and 3) the knowledge of persons of ordinary skill in the art. Respectfully, the motivation is simply not present from 1-3 above to arrive at Applicant's result as set out above, and full reconsideration therefore is respectfully requested. Clearly, the conclusion the Examiner has reached is a 20/20 hindsight reconstruction and improper. Applicant's claims set out above, clearly distinguish over the reference Illum. Clearly, the Examiner is expecting one of ordinary skill in the art to read Illum and to identify each of the steps set out above and to therefore arrive at Applicant's invention which is clearly patentable, and is set out below.

1. *"A pharmaceutical composition in the form of an emulsion preconcentrate comprising a cyclosporin dissolved in a solvent comprising acetylated monoglycerides, a hydrophilic organic solvent and a surfactant."*

and

15. *"A pharmaceutical composition in the form of an emulsion preconcentrate comprising a cyclosporin dissolved in acetylated monoglyceride lipophilic solvent, and a surfactant."*

Clearly Illum does not teach the use of acetylated monoglycerides as lipophilic solvents, nor does the reference suggest that it will work with cyclosporin in a preconcentrate. Nowhere in Illum is there taught that acetylated monoglycerides are good lipophilic solvents for cyclosporin because they are more easily dispersible in water.

The Examiner therefore, clearly has created an improper hindsight reconstruction relying heavily on Applicant's teachings and then dissecting

Illum to find those teachings and where those teachings are lacking as set out in the Examiner's Action of October 3, 2000 the man of ordinary skill in the art must therefore have an unreasonably high level of skill in the art to:

Item 1 – Select acetylated monoglycerides as a lipophilic solvent following determination or having prior knowledge that it will work with the cyclosporin in a preconcentrate which is self-emulsifying.

Item 2 – Be motivated to use the acetylated monoglycerides to dissolve the cyclosporin allegedly having knowledge that acetylated monoglycerides are formulated to enhance the solubility of cyclosporin, wherein the prior art Illum does not teach this fact. How can the man skilled in the art arrive at this conclusion?

Item 3 – Somehow having the knowledge that acetylated monoglycerides are a good solvent for cyclosporin also having the knowledge that in fact enhances dispersion of the material in water.

Item 4 – Having a reasonable expectation of success of all of the above steps which are not taught in Illum.

The Examiner therefore is relying in fact heavily on the level of knowledge of one of ordinary skill in the art, and very little on the teachings of Illum. Respectfully, this is improper and full reconsideration is requested.

In view of the above submissions, Applicant respectfully submits that the claims 1, and 15 through 21 in this Application are clearly allowable over the prior art Illum et al.

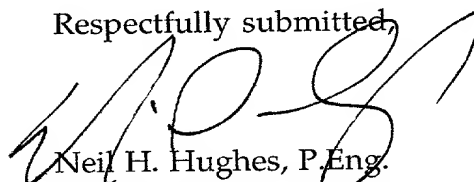
Enclosed is a cheque in the amount of \$980.00 U.S. which includes \$710.00 for the base filing fee of a large entity and \$270.00 for the multiple dependent claims. If there should occur an overpayment or an underpayment of fees in respect of this application, the Commissioner is authorized to access Deposit Account Number 08-3255 to make the appropriate adjustments and advised Applicants' Agent.

Attached hereto as Exhibit A (page 21 of this amendment) is a marked-up version of the changes made to the claims by the present voluntary amendment. The attached page is entitled **"EXHIBIT A - CLAIMS WITH MARKINGS TO SHOW CHANGES"**.

Also attached hereto as Exhibit B (pages 22 and 23 of this amendment) are two sheets that contains a clean set of all pending claims following entry of this amendment. These sheets are entitled **"EXHIBIT B - CLEAN SET OF ALL PENDING CLAIMS FOLLOWING ENTRY OF THE PRESENT VOLUNTARY AMENDMENT"**. All of the currently pending claims are consolidated in this list for the convenience of the Examiner.

If the Examiner has any questions, she is respectfully requested to contact Applicants' Agent, Neil H. Hughes at (905) 771-6414 at her convenience.

Respectfully submitted,



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Enclosures

Continuation Application of
Parent Application Serial No. 09/403,660
Group Art Unit 1615

Amendment A

EXHIBIT A

CLAIMS WITH MARKINGS TO SHOW CHANGES

15. A pharmaceutical composition in the form of an emulsion preconcentrate comprising a cyclosporin dissolved in acetylated monoglyceride lipophilic solvent, and a surfactant.

16. The composition of claim 1 or 15 in the form of a microemulsion preconcentrate.

17. The composition of claim 1 or 15 wherein the acetylated monoglyceride is a fully acetylated monoglyceride prepared from unsaturated monoglyceride.

18. The composition of claim 1 or 15 wherein the surfactant is selected from the group of a polyoxyethylene glycolated natural , hydrogenated vegetable oil, polyoxyl 40 hydrogenated castor oil, and a polyoxyethylene-sorbitan-fatty ester.

19. The composition of claim 1 or 15 comprising two surfactants, one of which is a polyoxyethylene glycolated natural or hydrogenated vegetable oil and the second of which is a polyoxyethylene-sorbitan-fatty acid ester.

20. The composition of claim 15 further comprising a hydrophilic organic solvent miscible with the acetylated monoglyceride lipophilic solvent.

21. The composition of claim 20 wherein said hydrophilic organic solvent is selected from the group of ethanol, propylene glycol, propylene carbonate, benzyl alcohol, and polyethylene glycol having mean molecular weight of less than about 1000.

Continuation Application of
Parent Application Serial No. 09/403,660
Group Art Unit 1615

Amendment A

EXHIBIT B

CLEAN SET OF ALL PENDING CLAIMS

FOLLOWING ENTRY OF THE PRESENT AMENDMENT

1. A pharmaceutical composition in the form of an emulsion preconcentrate comprising a cyclosporin dissolved in a solvent system comprising acetylated monoglycerides, a hydrophilic organic solvent and a surfactant.
15. A pharmaceutical composition in the form of an emulsion preconcentrate comprising a cyclosporin dissolved in acetylated monoglyceride lipophilic solvent, and a surfactant.
16. The composition of claim 1 or 15 in the form of a microemulsion preconcentrate.
17. The composition of claim 1 or 15 wherein the acetylated monoglyceride is a fully acetylated monoglyceride prepared from unsaturated monoglyceride.
18. The composition of claim 1 or 15 wherein the surfactant is selected from the group of a polyoxyethylene glycolated natural, hydrogenated vegetable oil, polyoxyl 40 hydrogenated castor oil, and a polyoxyethylene-sorbitan-fatty ester.
19. The composition of claim 1 or 15 comprising two surfactants, one of which is a polyoxyethylene glycolated natural or hydrogenated vegetable oil and the second of which is a polyoxyethylene-sorbitan-fatty acid ester.
20. The composition of claim 15 further comprising a hydrophilic organic solvent miscible with the acetylated monoglyceride lipophilic solvent.

21. The composition of claim 20 wherein said hydrophilic organic solvent is selected from the group of ethanol, propylene glycol, propylene carbonate, benzyl alcohol, and polyethylene glycol having mean molecular weight of less than about 1000.